10

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,408	03/21/2001	Simon Delagrave	HER-0041	2931

7590 05/06/2004

WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE 46TH FLR.
PHILADELPHIA, PA 19103

EXAMINER	
TRAN, MY CHAU T	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,408	DELAGRAVE ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/20/04 has been entered.

Status of Claims

1. Applicant's amendment filed 1/20/04 is acknowledged and entered. Claim 22 has been canceled. Claim 16 has been amended.

2. Claims 11-21 are rejoined with the elected invention of claims 1-9 in view of the amendment of claim 11, filed 6/26/03.

3. Claims 10, and 23-56 are canceled by the amendment filed on 6/26/03.

4. Claims 1-9, and 11-21 are pending.

Withdrawn Rejections

5. In view of applicant's amendments of claim 16, the previous rejection under 35 USC 112, second paragraph, has been withdrawn.

6. In view of applicant's arguments, the rejection of claims 1-2, 4-6, and 8-9 under 35 USC 102(e) as anticipated by Barany et al. (US Patent 6,506,594 B1) has been withdrawn.

7. In view of applicant's arguments, the rejection of claims 1-2, and 4-5 under 35 USC 102(e) as anticipated by Harney (Us Patent 6,495,318 B2) has been withdrawn.

8. In view of applicant's arguments, the rejection of claims 1, 4-5, 7-8, and 11-15 (*rejoined claims*) under 35 USC 102(e) as anticipated by Huang et al. (US Patent 6,489,466 B2) has been withdrawn.

9. In view of applicant's arguments, the rejection of claims 1-5, 7-9, and 11-19 (*rejoined claims*) under 35 USC 102(e) as anticipated by Delagrave (US Patent 6,479,262 B1) has been withdrawn.

10. In view of applicant's arguments, the rejection of claims 1, and 4-9 under 35 USC 103(a) as being obvious over Huang et al. (US Patent 6,489,466 B2) in view of Harney (Us Patent 6,495,318 B2) has been withdrawn.

11. In view of applicant's arguments, the rejection of claims 1 and 11-21 under 35 USC 103(a) as being obvious over Delagrave (US Patent 6,479,262 B1) and Barany et al. (US Patent 6,506,594 B1) has been withdrawn.

12. Claims 1-9, and 11-21 are treated on the merit in this Office Action.

Maintained Rejections

Double Patenting

13. Claims 1-5, 7-8, 11-15 (*rejoined claims*), and 17-18 (*rejoined claims*) are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of U.S. Patent No. 6,479,262 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the presently claimed invention, which is a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides, would encompass that of the claimed invention of US Patent 6,479,262 B1, which is a method of preparing a polynucleotide having at least 200 nucleotides and a predetermined nucleotide sequence. The method step comprises contacting said solid support with the 3′ terminus of a fist oligonucleotide from said plurality of oligonucleotides to form a tethered oligonucleotide, ligating the 3′ terminus of another oligonucleotide from said plurality of oligonucleotides to the 5′ terminus of the tethered oligonucleotide, phosphorylating the 5′ terminus of said another oligonucleotide, and repeating the steps of ligation and phosphorylation until said polynucleotide is prepared.

Response to Arguments

14. Applicant's argument(s) directed to the above rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7, 10, 12, 14,

18, and 24-26 of U.S. Patent No. 6,479,262 B1 were considered but they are not persuasive for the following reasons.

Applicant argues that the obviousness-type double patenting rejection of claims 1-5, 7-8, 11-15 (*rejoined claims*), and 17-18 (*rejoined claims*) as being unpatentable over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of U.S. Patent No. 6,479,262 B1 (Delagrave) is improper because Delagrave does not teach "[t]he coupled oligonucleotide resulting from the coupling step shares at least one terminal region of sequence with at least one other coupled oligonucleotide". Applicant define that "[A] shared terminal region of sequence refers to a region of the nucleotide sequence of *coupled* oligonucleotide #1 that also is present in coupled oligonucleotide #2, not that the ends of the oligonucleotides to be joined are shared upon coupling by virtue of, for example, ligation, or that the nucleotide sequence of the ends of the coupled oligonucleotides are complementary. For example, coupled oligonucleotide #1 comprising G1-G2 and coupled oligonucleotide G2-G3 share a terminal region of sequence, G2 (see specification, for example, at Figures 1 and 2)".

Applicant's arguments are not convincing since the obviousness-type double patenting rejection of claims 1-5, 7-8, 11-15 (*rejoined claims*), and 17-18 (*rejoined claims*) as being unpatentable over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of U.S. Patent No. 6,479,262 B1 (Delagrave) is proper. The limitation of 'wherein each of the coupled oligonucleotides shares at least one terminal region of sequence with at least one other coupled oligonucleotide' base on applicant definition (i.e. coupled oligonucleotide #1 is G1-G2 and couple oligonucleotide #2 is G2-G3 and thus shared share a terminal region of sequence, G2) would be a choice of experimental design and is considered within the purview of the cited prior art. Thus the

polynucleotide made by the method of claim 1, 10, and 20 of U.S. Patent No. 6,479,262 B1 (Delagrave) would be obvious over the polynucleotide made by the presently claim method and the obviousness-type double patenting rejection is proper.

New Rejections

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1-2, 4-9, 11-15, 17, and 19-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunkapiller et al. (US Patent 5,942,609).

Hunkapiller et al. disclose the method for assembly of a polynucleotide on a support (Abstract; col. 3, line 36 to col. 4, line 32). The method comprises the steps of immobilizing the

oligonucleotides on solid supports (col. 8, lines 64-66), coupling the oligonucleotides by way of ligation reaction (i.e. chain extension) (col. 10, lines 1-13), and the immobilized ligation products are amplified by polymerase chain reaction (col. 14, lines 47-48). The support includes materials such as agarose, and polystyrene (col. 9, lines 8-13). The immobilization occurs at the 3′ end of oligonucleotide (i.e. blocking at the 3′ end) (col. 9, lines 27-31). The length of the oligonucleotide includes the range of 20 to 200 bases (col. 13, lines 60-65).

The method of Hunkapiller et al. does not expressly disclose that the each coupled oligonucleotides shares at least one terminal region of sequence with at least one other coupled oligonucleotide and that the PCR is an overlap PCR.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include an overlap PCR and to design the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide in the method of Hunkapiller et al. One of ordinary skill in the art would have been motivated to include an overlap PCR and to design the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide in the method of Hunkapiller et al. because the type of PCR use and designing the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide would be a choice of experimental design and is considered within the purview of the cited prior art. Furthermore, one of ordinary skill in the art would have reasonably expectation of success in including an overlap PCR and designing the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide in the method of Hunkapiller et al. since the taught method would need no modification other than choosing the

type of PCR to use and the design of the coupled oligonucleotide that do not materially affect the method steps in producing an assemble polynucleotide.

18. Claims 1-9, 11-15, and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunkapiller et al. (US Patent 5,942,609) and Walker et al. (*PNAS*, **1975**, 72(1):122-126).

Hunkapiller et al. disclose the method for assembly of a polynucleotide on a support (Abstract; col. 3, line 36 to col. 4, line 32). The method comprises the steps of immobilizing the oligonucleotides on solid supports (col. 8, lines 64-66), coupling the oligonucleotides by way of ligation reaction (col. 10, lines 1-13), and the immobilized ligation products are amplified by polymerase chain reaction (col. 14, lines 47-48). The support includes materials such as agarose, and polystyrene (col. 9, lines 8-13). The immobilization occurs at the 3′ ends of oligonucleotide (col. 9, lines 27-31). The length of the oligonucleotide includes the range of 20 to 200 bases (col. 13, lines 60-65). Furthermore, the type of PCR and the design of the coupled oligonucleotides (i.e. each coupled oligonucleotides shares at least one terminal region of sequence with at least one other coupled oligonucleotide) would be a choice of experimental design and is considered within the purview of the cited prior art as discuss above.

The method of Hunkapiller et al. does not expressly include the T4 RNA ligase.

Walker et al. disclosed a method of joining single-stranded oligonucleotides using T4 RNA ligase (Abstract). The RNA ligase has the advantage of not requiring the complementary strand, thereby simplifying the synthetic task (pg. 126, right col., lines 1-2).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the T4 RNA ligase as taught by Walker et al. in the method of

Barany et al. One of ordinary skill in the art would have been motivated to include the T4 RNA ligase in the method of Barany et al. for the advantage of not requiring the complementary strand, thereby simplifying the synthetic task (Walker: pg. 126, right col., lines 1-2) since both Barany et al. and Walker et al. disclose a method of coupling oligonucleotides by the method of ligation (Barany: col. 5, lines 33-41; Walker: Abstract). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Hunkapiller et al. and Walker et al. because Walker et al. disclosed joining two single-stranded oligomers using T4 RNA ligase (Walker: Abstract; pg. 124).

19. Claims 1-4, 6-9, 11-13, and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyman (US Patent 5,602,000).

Hyman discloses a method disclose the method for assembly of a polynucleotide via enzymatic synthesis of oligonucleotides (Abstract; col. 3, lines 22-48). The method comprises the steps of blocking the 3′ ends of oligonucleotide with a nucleotide substrate (col. 10, lines 56-63), coupling the oligonucleotides by way of ligation reaction using RNA ligase (i.e. chain extension) (col. 8, lines 58-63), and amplifying the extended oligonucleotide via polymerase chain reaction (col. 6, line 65 to col. 7, lines 3). The type of RNA ligase is T4 RNA ligase (col. 9, lines 41-50). The length of the oligonucleotides includes 25 bases (col. 13, lines 59-60).

The method of Hyman does not expressly disclose that the each coupled oligonucleotides shares at least one terminal region of sequence with at least one other coupled oligonucleotide and that the PCR is an overlap PCR.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include an overlap PCR and to design the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide in the method of Hyman. One of ordinary skill in the art would have been motivated to include an overlap PCR and to design the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide in the method of Hyman because the type of PCR use and designing the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide would be a choice of experimental design and is considered within the purview of the cited prior art. Furthermore, one of ordinary skill in the art would have reasonably expectation of success in including an overlap PCR and designing the coupled oligonucleotides to share at least one terminal region of sequence with at least one other coupled oligonucleotide in the method of Hyman since the taught method would need no modification other than choosing the type of PCR to use and the design of the coupled oligonucleotide that do not materially affect the method steps in producing an assemble polynucleotide.

20. Claims 1-4, 6-9, 11-13, and 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hyman (US Patent 5,602,000) and Langer et al. (*PNAS*, **1981**, 78(1):6633-6637).

Hyman discloses a method disclose the method for assembly of a polynucleotide via enzymatic synthesis of oligonucleotides (Abstract; col. 3, lines 22-48). The method comprises the steps of blocking the 3′ ends of oligonucleotide with a nucleotide substrate (col. 10, lines 56-

63), coupling the oligonucleotides by way of ligation reaction using RNA ligase (i.e. chain extension) (col. 8, lines 58-63), and amplifying the extended oligonucleotide via polymerase chain reaction (col. 6, line 65 to col. 7, lines 3). The type of RNA ligase is T4 RNA ligase (col. 9, lines 41-50). The length of the oligonucleotides includes 25 bases (col. 13, lines 59-60). Furthermore, the type of PCR and the design of the coupled oligonucleotides (i.e. each coupled oligonucleotides shares at least one terminal region of sequence with at least one other coupled oligonucleotide) would be a choice of experimental design and is considered within the purview of the cited prior art as discuss above.

The method of Hyman does not expressly include biotin-dideoxyuridine triphosphate as a blocking group.

Langer et al. disclose the method of DNA and RNA polymerases using biotin-labeled nucleotides as a substrate (Abstract; pg. 6633, left col., line 30 to right col., line 21). The biotin-labeled nucleotide is a biotin-dideoxyuridine triphosphate (pg. 6633, right col., lines 9-21).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include biotin-dideoxyuridine triphosphate as a blocking group as taught by Langer et al. in the method of Hyman. One of ordinary skill in the art would have been motivated to include biotin-dideoxyuridine triphosphate as a blocking group in the method of Hyman for the advantage of providing a simple and rapid procedure for synthesizing chemically stable biotin-substituted polymers that hybridized specifically and efficiently to complementary sequences either in solution or bound to solid support (Langer: pg. 6637, left col., lines 7-13) since both Hyman and Langer et al. disclose the method of DNA polymerase using nucleotide substrate (Hyman: Abstract; col. 10, lines 56-63; Langer: Abstract; pg. 6633, left col., line 30 to

right col., line 21). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Hyman and Langer et al. because Langer et al. disclose enzymatic polymerization of nucleotides using biotin-labeled nucleotides as a substrate (pg. 6635, left col., lines 1-28).

Double Patenting

21. Claims 1-9, and 11-21 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 7-9, 11-14, and 17-22 of U.S. Patent No. 6,635,453 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the presently claimed method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides and the patented method of preparing a polynucleotide from a plurality of oligonucleotides comprises the method steps of blocking the 3′ end of the oligonucleotide with a blocking group such as a solid support or biotin-dideoxyuridine triphosphate, coupling the 5′ ends of the oligonucleotide with another oligonucleotide via T4 RNA ligase, and amplifying the coupled oligonucleotides to produce the polynucleotide. Furthermore, the type of PCR and the design of the coupled oligonucleotides (i.e. each coupled oligonucleotides shares at least one terminal region of sequence with at least one other coupled oligonucleotide) would be a choice of experimental design and is considered within the purview of the cited prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
May 3, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER